REMARKS/ARGUMENTS

Claims 1-26 and 29-40 remain in this application.

Claims 6-10, 17-21 and 29-40 stand withdrawn as the result of an earlier restriction requirement.

In view of the examiner's earlier restriction requirement, applicant retains the right to present claims 6-10, 17-21 and 29-40 in a divisional application.

In response to the Office Action of December 6, 2006, Applicant requests re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

Requirement for Election/Restriction:

The Examiner's consideration of Applicants' previous response to the Requirement for Restriction/Election (see paragraphs 1-11 of the instant Office action) are duly noted.

Claims 1-5, 11-16, and 22-28 are understood to be currently under consideration.

Claims 27 and 28 are cancelled via the instant amendment.

Rejections under 35 USC 112 - second paragraph

Claims 1-5, 11, and 23-28 stand rejected as being indefinite because claims 1 and 23 recite the phrase "identifying characteristics".

Accordingly, this language has been removed from the claim.

The claims have been modified to identify the antibody as being an isolated monoclonal antibody or antigen binding fragment thereof which has *in vitro* cytotoxic properties against malignant tumor cells and identifies the region bound by the isolated monoclonal antibody or antigen binding fragments thereof, which is the subject of the claims, as the extracellular region encompassing amino acids 108-202 of CD63, which region is bound by the isolated monoclonal antibody produced by the hybridoma cell line deposited with the ATCC as PTA-4890. Basis for these amendments may be found in the originally filed disclosure at pages 21, l.1-9, p. 22, l.1-5 and page 40, l. 21-23.

Claims 1-5 and 11 are rejected as being indefinite because claim 1 is drawn to administering an anti-cancer antibody or fragment thereof, which encompasses the Fc and antigen binding fragments, and is also drawn to said antibody being an isolated monoclonal antibody or antigen binding fragment thereof. It is unclear if the claims are encompassing both antibody fragments which bind to a target antigen, i.e. the antigen binding fragments, and fragments that would not bind to the target antigen, i.e. the

Fc region of the antibody. Thus, the metes and bounds of the claim cannot be determined.

Accordingly, the claims have been amended to specify "antigen binding fragments" throughout.

Claims 2, 4, 13, 15, 24, and 26 are rejected as being indefinite because it recites the phrase a "chimerized antibody". The claims have been modified to state that the antibody is "chimeric". The exact meaning of a chimeric antibody is well-known. The process for engineering antibodies, whether humanized or chimeric, is well-described, for example the reference to Winter et al (of record) describes first generation humanized antibodies as simple chimeric mAbs. It is submitted that given the state of the art, such terminology is understood, and such antibodies are obtainable through routine experimentation of a skilled artisan. Thus the metes and bounds of the claim protection sought are readily determined, and it is respectfully requested that this ground of rejection be withdrawn.

Claims 1-5, 11-16, and 22 stand rejected as being indefinite because claims 1 and 12 recite the phrase "essentially benign".

Accordingly, this language has been removed from the claims.

Claim 15 is rejected for reciting the limitation "said subset". There is insufficient antecedent basis for this limitation in claim 14 from which claim 15 depends.

Accordingly, this limitation has been deleted from the claim.

Claim 28 recites the limitation "humor tumor tissue sample" in claim 23.

Claim 28 has been canceled, thus obviating this ground of rejection.

Rejections under 35 USC 112 - first paragraph

Claims 23-29 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) are alleged to contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a process for mediating cytotoxicity of a human tumor cell which expresses a CD63 antigenic moiety on the cell surface comprising: contacting said tumor cell with an isolated monoclonal antibody or antigen binding fragment thereof, said antibody or antigen binding fragment thereof being an isolated monoclonal antibody or

antigen binding fragment thereof which binds to said expressed CD63 antigenic moiety, said antigenic moiety characterized as being bound by an antibody having the identifying characteristics of a monoclonal antibody encoded by the clone deposited with the ATCC as PTA-4890, whereby cell cytotoxicity occurs as a result of said binding.

The monoclonal antibody encoded by the clone deposited with the ATCC as PTA-4890, also referred to in the specification as 7BD-33-11A, will be referred to as PTA-4890.

The specification teaches, based on mass spectroscopic identification combined with the confirmatory immunoprecipitation, western blotting experiments using known CD63 antibodies, and testing the reactivity of PTA-4890 against different isolated extracellular domains of CD63, that the antigen for PTA-4890 is CD-63 and PTA-4890 binds the extracellular region of CD63 encompassing amino acids 108-202, see p. 40, lines 21-23, Example 2, and Fig. 4-9

The specification teaches that PTA-4890 was specifically cytotoxic in breast and prostate tumor cell lines selectively, and did not affect normal cells in *in vitro* assays, see p. 42, lines 20-22 and Table 1. The specification teaches that PTA-4890 had cytotoxic activity against the breast cancer cell lines MCF-7 and PC-3 prostate cancer cell line, but not the

MDA-MB-468, MDAMB-231, HT-29, SW116, SW620, NCI H460 tumor cell lines, see Table 1.

The specification teaches that PTA-4890 displayed specific tumor binding to the MCF-7, PC-3, MDA-MB-468, MDA-MB-231, HT-29, SW116, SW620, and NCI H460 and other tumor cell lines, see Table 2. The specification teaches that there was also binding of PTA-4890 to non-cancer cells, however that binding did not produce cytotoxicity. The specification teaches that this was further evidence that binding was not necessarily predictive of the outcome of antibody ligation of its cognate antigen, and was a non-obvious finding. The specification teaches that this suggested that the context of antibody ligation in different cells was determinative of cytotoxicity rather than just antibody binding, see para. bridging p. 44 and 45.

Applicant is in agreement with the Examiner's analysis.

The claims have thus been amended to be limited to treating a patient suffering from **human breast or prostate cancer** or for mediating cytotoxicity of **a human breast or prostate tumor cell** with a monoclonal antibody or antigen binding fragment thereof which **has *in vitro* cytotoxic properties against malignant tumor cells and** binds to an extracellular region encompassing amino acids 108-202 of CD63 expressed by said breast or prostate cancer, which

region is bound by the isolated monoclonal antibody produced by the hybridoma cell line deposited with the ATCC as PTA-4890.

Basis for these amendments in the original disclosure is outlined *supra*.

The additional similar grounds of rejection under 35 USC 112 are likewise deemed to be obviated by the instant amendments.

Claims 1, 3, 5, 11, 12, 14, 16, 22, 23, 25, and 27 stand rejected under 35 U.S.C. 112, first paragraph, because the Examiner alleges that the specification, while being enabling for a method for treating a patient suffering from a cancerous disease or for a process for mediating cytotoxicity with a monoclonal antibody encoded by the clone deposited with the ATCC as PTA-4890, wherein said antibody is a **humanized** antibody, does not reasonably provide enablement for a method for treating a patient suffering from a cancerous disease or for a process for mediating cytotoxicity of a human tumor cell with a monoclonal antibody having the identifying characteristics of a monoclonal antibody encoded by the cloned deposited with the ATCC as PTA-4890, wherein said antibody is a **murine** antibody. The Examiner alleges that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

It is respectfully submitted that the Examiner is ignoring the demonstrated utility of the isolated monoclonal antibodies and antigen binding fragments thereof, which are the subject of the instant claims, and instead implying a test of long-term efficacy and immunogenicity in humans, which is not the subject of the claims.

The claims read on treating a patient suffering from human breast or prostate cancer, or alternatively a method for mediating cytotoxicity of **a human breast or prostate tumor cell** with a monoclonal antibody or antigen binding fragment thereof which **has *in vitro* cytotoxic properties against malignant tumor cells and** binds to an extracellular region encompassing amino acids 108-202 of CD63 expressed by said breast or prostate cancer, which region is bound by the isolated monoclonal antibody produced by the hybridoma cell line deposited with the ATCC as PTA-4890 with a mouse monoclonal antibody PTA-4890.

This means that the claims read on, and the specification contemplates, the treatment of human breast or prostate cancer with antibodies produced in a mouse, or alternatively with humanized or chimeric versions thereof.

Even the reference to Winter et al, cited by the Examiner, admits to the utility of such mouse derived antibodies, and Applicants are justified in seeking claim protection for that

utility. Winter states that such unwanted responses as a HAMA reaction can develop. But even humanization does not preclude such development of untoward responses, as illustrated by Winter at p. 141, column 2, with respect to treatment of RA patients. Such determinations are made in the clinic, which is why expensive staged clinical trials of biologics are routinely carried out.

The statutory test of 35 USC 112 1st paragraph, as instantly applied by the Examiner, is respectfully submitted to improperly attempt to deny Applicants their rightful claim to the recognized and demonstrated utility of the unique isolated monoclonal antibodies or antigen binding fragments thereof as described herein.

It is therefore respectfully submitted that this ground of rejection be withdrawn.

It is further submitted that the claims, as presently submitted, meet the test of Lilly and that the specification, as outlined *supra* provides an adequate written description of the claimed characteristics of the isolated monoclonal antibody or antigen binding fragments thereof that are required to practice the claimed invention.

Double Patenting Rejections

Claim 1-5, 12-16, and 23-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-12 and 14-16 of U.S. Patent No. 7,009,040 in view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New York, 1990, p. 507), and in further view of Miller and Tannock (The Basic Science of Oncology, 2nd ed., McGraw- Hill Inc., 1992, Ch.14).

Claims 1, 12, 23, and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 5 and 6 of copending Application No. 11/321,624, in view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New York, 1990, p. 507), and in further view of Miller and Tannock (The Basic Science of Oncology, 2nd ed., McGraw- Hill Inc., 1992, Ch.14).

Claims 1, 12, 23, and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 56 and 57 of copending Application No. 11/362,452 in view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New York, 1990, p. 507), and in further view of Miller and Tannock (The Basic Science of Oncology, 2nd ed., McGraw- Hill Inc., 1992, Ch.14).

Claims 1-5, 12-16, and 23-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 6-8 and 10 of copending Application No. 11/370,203 in view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New York, 1990, p. 507), and in further view of Miller and Tannock (The Basic Science of Oncology, 2nd ed., McGraw- Hill Inc., 1992, Ch.14).

Claims 1, 12, 23, and 27 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 56 and 57 of copending Application No. 11/367,798 in view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New York, 1990, p. 507), and in further view of Miller and Tannock (The Basic Science of Oncology, 2nd ed., McGraw- Hill Inc., 1992, Ch.14).

Claims 1-5, 12-16, and 23-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 and 6-8 of copending Application No. 11/462,092 in view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New York, 1990, p. 507), and in further view of Miller and Tannock (The Basic Science of Oncology, 2nd ed., McGraw- Hill Inc., 1992, Ch.14).

Claims 1-5, 12-16, and 23-27 are rejected on the ground of nonstatutory obviousness-type double patenting as being

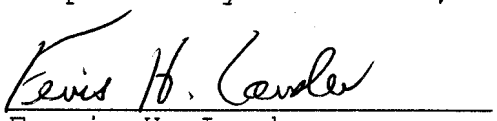
unpatentable over claims 1-3, 5-10, 12-16 of copending Application No. 11/493,407 (11/493,047 erroneously noted by the Examiner in the Office Action) in view of Kimball (Introduction to Immunology, 3rd ed. Macmillan, Inc, New York, 1990, p. 507), and in further view of Miller and Tannock (The Basic Science of Oncology, 2nd ed., McGraw- Hill Inc., 1992, Ch.14).

Accordingly, Terminal Disclaimers are submitted herewith to obviate each of the above double patenting rejections.

SUMMARY

In light of the foregoing remarks and amendment to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested. The Examiner is requested to contact the undersigned by telephone, to clarify any issues not herein resolved, in order to expedite prosecution.

Respectfully submitted,



Ferris H. Lander
Registration # 43,377

McHale & Slavin, P.A.
2855 PGA Boulevard
Palm Beach Gardens, FL 33410
(561) 625-6575 (Voice)
(561) 625-6572 (Fax)